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Lead exposure in young children over a 5-year period from urban environments using alternative exposure measures with the US EPA IEUBK model – A trial

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ABSTRACT

The US Environmental Protection Agency (EPA) Integrated Exposure Uptake Biokinetic (IEUBK) model has been widely used to predict blood lead (PbB) levels in children especially around industrial sites. Exposure variables have strongly focussed on the major contribution of lead (Pb) in soil and interior dust to total intake and, in many studies, site-specific data for air, water, diet and measured PbB were not available. We have applied the IEUBK model to a comprehensive data set, including measured PbB, for 108 children monitored over a 5-year period in Sydney, New South Wales, Australia. To use this data set, we have substituted available data (with or without modification) for standard inputs as needed. For example, as an alternative measure for soil Pb concentration (μg/g), we have substituted exterior dust sweepings Pb concentration (μg/g). As alternative measures for interior dust Pb concentration (μg/g) we have used 1) 30-day cumulative petri dish deposition data (PDD) (as μg Pb/m^2/30days), or 2) hand wipe data (as μg Pb/hand). For comparison, simulations were also undertaken with estimates of dust Pb concentration derived from a prior regression of dust Pb concentration (μg/g) on dust Pb loading (μg/ft^2) as concentration is the unit specified for the Model. Simulations for each subject using observed data aggregated over the 5-year interval of the study, the most usual application of the IEUBK model, showed using Wilcoxon tests that there was a significant difference between the observed values and the values predicted by the Model containing soil with hand wipes ($p < 0.001$), and soil and PDD ($p = 0.026$) but not those for the other two sets of predictors, based on sweepings and PDD or sweepings and wipes. Overall, simulations of the Model using alternative exposure measures of petri dish dust (and possibly hand wipes) instead of vacuum cleaner dust and dust sweepings instead of soil provide predicted PbB which are generally consistent with each other and observed values. The predicted geometric mean PbBs were 2.17 (± 1.24) μg/dL for soil with PDD, 1.95 (± 1.17) μg/dL for soil with hand wipes, 2.36 (± 1.75) μg/dL for sweepings with PDD, and 2.15 (± 1.69) for sweepings with hand wipes. These results are in good agreement with the observed geometric mean PbB of 2.46 (± 0.99) μg/dL. In contrast to all other IEUBK model studies to our knowledge, we have stratified the data over the age ranges from 1 to 5 years. The median of the predicted values was lower than that for the observed values for every combination of age and set of measures; in some cases, the difference was statistically significant. The differences between observed and predicted PbB tended to be greatest for the soil plus wipes measure and for the oldest age group. Use of 'default dust' values calculated from the site-specific soil values, a common application of the IEUBK model, results in predicted PbB about 22% (range 0 to 52%) higher than those from soil with PDD data sets. Geometric mean contributions estimated from the Model to total Pb intake for a child aged 1–2 years was 0.09% for air, 42% for diet, 5.3% for water and 42% for soil and dust. Our results indicate that it is feasible to use alternative measures of soil and dust exposure to provide reliable predictions of PbB in urban environments.

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1. Introduction

The US EPA IEUBK model has been the regulatory model of choice in developing site-specific cleanup levels, especially in highly to moderately contaminated sites such as former smelters or mining locations. This Model evaluates the risks to children aged 1 to 6 years from exposure to Pb in environmental media including outdoor soil, indoor dust, air, water and diet. Ingestion and inhalation of fine soil and dust particulates are the dominant sources and pathways of lead exposure in young children. House dust is a significant contributor to PbB levels in children (Bornschein et al., 1985; Charney et al., 1980; Duggan, 1983; Duggan and Inskip, 1985; Fergusson and Kim, 1991; Gulson et al., 1995, 2013; Laidlaw et al., 2014; Landrigan et al., 1976; Lanphear et al., 1995, 1996, 1998a, 1998b, 1997; Laxen et al., 1987; Mielke et al., 1997, 2010; Thornton et al., 1990; von Lindern et al., 2003a, 2003b and references therein). Individual behaviour, exposure interval and environmental conditions such as season are key factors in a child's exposure (Laidlaw et al., 2014; Zahran et al., 2013a). Although widely used and evaluated in industrial areas there has been limited application of the IEUBK model to urban environments even though there have been several major investigations, especially in the US, relating PbB levels to remediation programs focussed mainly on lead paint removal and the use of soil and surface wipes as the critical media (US EPA, 2000; US HUD, 2017). For example, in a Medline search for IEUBK there were 33 references but only 5 were directed at non-industrial settings. In Australia, Health Investigation Levels (HIL) such as HILA A, a low density residential land use, have been established on the basis of the IEUBK model, with parameters adopted for the derivations of the HILs from National Environmental Protection Measures (NEPM 2013a, 2013b).

Because of the simplicity of collection, soil Pb concentration is generally measured at every location but indoor dust, usually collected by vacuum cleaning, is not always measured because of cost and invasiveness to the residents. When not collected, estimates of the Pb concentration in indoor dust are usually calculated from the observed Pb concentration in outdoor soil giving 'default' dust values (US EPA, 1994a). There has been considerable discussion over 2 decades about the suitability in the IEUBK model of surface dust from, for example surface wipes (e.g., Emond et al., 1997), as it is measured as Pb loading (µg Pb/ft^2 or µg Pb/m^2) whereas in the Model the input is as concentration. It is generally agreed that Pb loading is a more robust predictor of PbB than concentration (e.g., Milar and Mushak, 1982; Lanphear et al., 1995, 1998a) and in the earlier version (1.05) of US EPA Adult biokinetic model (AALM) there was the option to input dust as Pb loading. In the current beta version of AALM the dust exposure is input as µg/g and soil has been discarded. [The term "soil" has been discarded in place of "dust" to represent surface dusts from any source, including soil. the rationale for this is that the exposure pathway for soil is through surface dust (see references cited in this manuscript). This is consistent with U.S. EPA guidance to sample the top layers of soil (e.g., 5 cm) for estimating surface dust Pb concentration. It is also the rationale for U.S. HUD guidance for sampling surface dust with surface wipes. (Explanation courtesy of a reviewer)].

In spite of large data sets available for surface wipe dust, especially through the agencies of US Housing and Urban Development (HUD) and US National Center for Healthy Housing, these data sets have rarely been trialled in the IEUBK model to our knowledge, perhaps because of the focus on cleanup guidelines after paint remediation.

Besides dust sampling using vacuum cleaners or surface wipes, both of which have deficiencies (Gulson and Taylor, 2017), for longitudinal studies a more robust method for dust exposure is dust fall accumulation using trays (Angle et al., 1979; Clark et al., 1995; van Alphen, 1999) or petri dishes (Gulson and Taylor, 2017, and references therein) which provide a measure of dust accumulation over time rather than only metal concentrations and is a suggested proxy for vacuum cleaner dust. Likewise, a more direct measure of exposure is via hand wipes of the children (Buchet et al., 1980; Roels et al., 1980; Bornschein et al., 1985; Gulson et al., 2006; Manton et al., 2000; Viverette et al., 1996) and is a suggested proxy for surface wipes but this approach has been infrequently implemented possibly because of perceived inconvenience to the children and interpretation of the results.

We have used data from a 5-year longitudinal study (Gulson et al., 2006, 2014) which was to evaluate potential changes to the environment and exposure of young children associated with the introduction of methylcyclopentadienyl manganese tricarbonyl (MMT) to Australia in 2001. Samples of blood and urine and environmental materials were analysed for a suite of 20 elements using inductively coupled plasma methods resulting in ~7000 samples from 108 children. The aims of the current study were to employ the Pb data in the IEUBK model to determine the validity of using alternative measures of exposure of dust collected in petri dishes or by hand wipes, and exterior dust sweepings as a metric for soil. In contrast to all other studies known to us, we also stratified the data for modelling for each individual into the age ranges used in the IEUBK model. Finally, we compared the output from the IEUBK modelling with our earlier path or structural equation modelling using linear mixed model analyses (Gulson et al., 2014), a more sophisticated approach in which adjustments are possible for the different environmental measures as well as variables such as proximity to major traffic thoroughfares, season and gender.

2. Methods

Samples were collected at 6-monthly intervals at residences located at varying distances from major traffic thoroughfares in Sydney and in the surrounding suburbs and from children, whose age ranged from 0.29 to 2.4 years at the time of first sample collection.

2.1. Sampling

Soil samples and exterior dust sweepings (using dust pan and broom over ~1 m^2) from front and back areas around the houses were collected in zip-lock plastic bags at 6-month intervals to provide information on former and current deposition. Duplicates of the children's dietary intakes for 6 days were obtained during the same time periods as the environmental sampling (Shim et al., 2014). All food eaten within a 6-day time frame was sampled. Fully flushed drinking water samples were collected from the kitchen faucet. The protocols for sample collection and preparation are described in Gulson et al. (1997). Hand wipes for each hand of the children were collected into cleaned polyethylene centrifuge test tubes prior to, and after, the child played outdoors. Both hands front and back and each finger were wiped individually using a "Johnson & Johnson" baby wipe. Dustfall accumulation in two frequented areas of the house (child's bedroom, living/play room) were collected over 6-month periods by the petri-dish method (Gulson et al., 1995) to provide ongoing monitoring of dust Pb loadings (expressed as amount of Pb/area/time). Although other sites such as day care centres and exterior locations were also monitored, the data sets for these were not as comprehensive as the residence interior dust and have not been modelled separately. Venous blood samples from the same child for multiple years were collected by a trained paediatric phlebotomist into ultra-trace metal free Vacutainer tubes using a 23 G ¾ Vacutainer blood collection set consisting of 12″ tubing with multiple sample Luer adapter ("butterfly"). The child's weight at each visit was measured using portable electronic scales. A questionnaire was administered at the time of the first sampling and updated throughout the study. Information was obtained about the location of the residence with respect to traffic, age and condition of the residence, metal exposure, and more personal details relevant to the parents and child.

Details of sample preparation and analyses are given in Gulson et al. (2006).

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2.2. Data treatment

The data consisted of observations collected over varying periods for 108 participants from 100 residences. The number of observation-occasions ranged from 2 to 13 per subject, with a mean of 9. In order to assess variations in the relationship between observed and predicted values for children of different ages, six groups were created: under 1 year (n = 32), 1- < 2 years (91), 2- < 3 years (104), 3- < 4 years (86), 4- < 5 (61) and 5+ years (28). Not all children provided data for all age groups and some provided data collected at two different times in the same age group. In the latter case, the multiple observations were averaged in that age group.

For the purposes of longitudinal analyses, multiple imputation (Honaker et al., 2007; King et al., 2001) was used to fill in unavoidable gaps in the data, as described in Gulson et al. (2014). The analyses described here were not longitudinal and were based on the observed and imputed values averaged within individuals either over the full span of the study or within age groups.

As the data were highly positively skewed, the median and the interquartile range (IQR) were used as measures of central tendency, and analyses were based on non-parametric tests. For each measure, observed or imputed values which were five or more times the IQR above the 75th percentile were set to missing before the values were averaged within individuals. In assessing statistical significance of differences between the observed and predicted value, no adjustment was made for the number of comparisons between conditions, as the aim was to consider all possible discrepancies, and to allow Type II errors, rather than strictly controlling Type I error.

2.3. IEUBK modelling

We used version IEUBK win1-1 Build 11 to obtain predicted PbB levels with various data sets. We used site-specific data for all analyses apart from air values which were based on ≤ $PM_{2.5}$ measurements for 2 Sydney sites, one suburban and the other a rural location and were collected over the same time period of the MMT study (Cohen et al., 2006). However, the air values are very low (< 0.02 µg/m^3) and make an insignificant contribution to the PbB values (see later discussion). In contrast to the general use of the Model, whereby estimates of PbB are obtained for various ages (0–1, 1–2, 2–3, 3–4, 4–5, 5–6, 6–7 years), we organised our site-specific data into similar age ranges prior to running the Model. That is, there were different exposure data for each age range and each child. Concern has been expressed about the limited amount of data available for the 0–6 year age range (Peer Reviewers Question EPA Drinking Water Lead Modelling Approaches, INSIDEEPA.com, 2017, page 2). The environmental data were entered into the Model as measured: PDD data were entered as dust Pb loadings in µg Pb/m^2/30 days as well as being converted to concentrations for comparison (described below in Section 2.3.1), soil as mg/kg, dust sweepings as mg/kg, diet as µg/day, and air as µg/m^3. The hand wipe data were entered as µg Pb per hand wipe, although we recognise there are deficiencies in using the hand wipe data as reinforced by the reviewers. We evaluated a conversion of the hand wipe data to concentration as follows. If we assume a surface area for a child's hand based on literature values (e.g., US EPA Exposure factors handbook: 2011 edition) of say about 300 cm^2, (0.03 m^2) we obtain a value of ≤ 0.02 µg Pb/cm^2 which is not directly applicable to the Model but is compatible with the PDD data. However, these loading values for the hand wipe dust are so low that they make little difference to the simulations which are dominated by the soil values.

Some scientists disagree about whether an empirical (statistically based) or a mechanistic model (e.g., IEUBK) should be used to develop health-based standards or whether dust lead loading (µg of Pb per unit surface area) or dust Pb concentration (µg of Pb per gram of dust) should be used as the unit of measure for the dust standard (Lanphear et al., 1998a, 1998b). In their seminal 1998 paper, Lanphear et al. demonstrated that Pb loading data was more predictive of children's PbB levels than Pb concentration. Thus, all studies in their pooled analysis collected dust by using either wipes or a dust sampling method that was able to be converted to estimates of Pb loading as measured by wipe samples. The U.S. Department of Housing and Urban Development (HUD) earlier indicated a policy preference for dust lead loadings sampled with a wipe compared with those taken with a vacuum cleaner (US HUD, 1995). [The terms "empirical" & "mechanistic" should be used to describe results in terms of correlations (scatter plots) between environmental variables (empirical) and blood lead and differences (box plots) between predicted and observed blood lead levels (mechanistic), respectively].

2.3.1. Comparisons of dust loading and concentration

The main objective of our paper to evaluate whether we could obtain sensible predicted PbB values using alternative exposure media and alternative measured units, especially dust fall accumulation, instead of vacuum cleaner material. We initially input the PDD results as loading (µg/m^2/30 days). We recognised that concentration measurements were the unit for the Model and noted that in the Lanphear et al. (1998a, 1998b) paper there was mention of a conversion equation for indoor dust from loading to concentration. However, this was unavailable from the designated author. A reviewer alerted us to the dust Pb loading-concentration conversion model in a US EPA document (US EPA, 2007). The equation for the concentration to loading regression was:

$$\ln(\text{PbCONC}) = 40.92 + 00.52 \times \ln(\text{PbVAC}) \quad (1)$$

where: PbCONC = indoor dust concentration (µg/g); PbVAC = vacuum indoor dust Pb loading (µg/ft2).

The PDD loading data for individuals aggregated over the period of the study were converted to concentration using Eq. (1). To maintain consistency with the Model we converted our loading data from meters squared to foot squared to calculate the concentrations. Furthermore, we derived a loading/concentration factor ("Succop" factor) from the 10 studies reported in Table 1 of the Succop et al. (1998) paper where both interior dust Pb concentration and dust Pb loading were listed and applied this to our PDD loading data to obtain concentrations for use in the model. The loading/concentration values in the Succop et al. (1998) paper ranged from 0.21 to 0.65 with a geometric mean of 0.31. Besides the other simulations listed in Table 1 we ran simulations to compare with observed PbB values using (i) the dust **concentration** data aggregated for each individual over the period of the study, (ii) the dust **loading** data aggregated for each individual over the period of the study (as in simulation 1 in Table 1), (iii) the same data with the "Succop" factor applied to the loading data to obtain concentration, and (iv) observed and imputed data aggregated for each individual.

We also compared the loading and concentration simulations for the age stratified data reported in Section 3.2 and these results are given for the age group 2- < 3 years in Supplementary Fig. S1.

The main Model simulations were undertaken on the following data sets (Table 1).

3. Results and discussion

Approximately 90% of the houses were built prior to 1980 so there was the possibility of Pb paint being present in both exterior and interior uses. However, the occurrence of Pb paint was limited as the houses were dominantly brick construction. In spite of the ages of the houses, paint with concentrations above 1% Pb was found in 25 of the 100 houses and deteriorating paint was only observed in 4 houses. The contribution of Pb in paint to contamination is complicated as, in many cases, there had been renovations carried out by different owners over the life of the house. Renovations carried out in many of these houses resulted in contamination of soils and the residences and in some of these there was a strong correlation of PbB and soil and dust sweepings.

Table 1
IEUBK simulations in this paper.

Pb data source input to IEUBK	Nomenclature used in the paper
1. Observed data aggregated for each individual over the study period and PDD converted to concentration	1. Comparisons of dust loading and concentration (Section 3.1)
2. Observed data aggregated for each individual over the study period	2. Predicted vs observed PbB values for aggregated data (Section 3.2) ***Observed and predicted PbB values for different age groups*** (Section 3.3)
3. Observed & imputed Soil and PDD data aggregated for each age	3. Soil with PDD or Soil + PDD in figures
4. Observed & imputed Outdoor sweepings and PDD data aggregated for each age	4. Sweeps with PDD or Sweeps + PDD in figures
5. Observed & imputed Soil and hand wipes aggregated for each age	5. Soil with wipes or Soil + wipes in figures
6. Observed & imputed Sweepings and hand wipes aggregated for each age	6. Sweeps with wipes or Sweeps + wipes in figures
7. Artificial interior dust data generated from outdoor soil data per IEUBK	7. Default dust (Section 3.4)

Critical parameters in use of the IEUBK model are ingestion rates and bioavailability of the Pb from soil and dust and the importance of these have been recently reviewed by von Lindern et al. (2016). We used the default ingestion rates and bioavailability (30% for soil and dust) from the IEUBK model. Laidlaw et al. (2017) measured bioaccessibility in 18 soil samples (< 250 µm) from the Sydney urban area with calculated values for bioavailability of 34 ± 5% with a range of 25–43% but as these results are similar to the IEUBK default values we have retained the EPA numbers. Nevertheless, as the particle size for petri dish dust and dust on hand wipes is considerably smaller than for soils, and hence potentially more bioavailable, we have carried out repeat simulations on the data sets 3 to 5 in Table 1, at the suggestion of a reviewer, using a bioavailability of 50%. The geometric mean increases in predicted PbB in using a bioavailability of 50% instead of 30% is +0.88% for soil with wipes, + 7.2% for soil with PDD, and +6.6% for sweepings with PDD. These results are still slightly lower than for the geometric mean for the observed PbB but lie within the error limits.

Laidlaw et al. (2017) made the following statement about bioavailability in their Sydney soil study: "Assuming an absolute bioavailability of 34%, the IEUBK model predicts a geometric mean BLL of 2.0 ± 2.0 µg/dL with a range from 1.3 to 16.8 µg/dL (Table 3 and Fig. 3) with 5.6% of the predicted BLLs exceeding the NHMRC (2015) reference level for lead in blood of 5 µg/dL and 2.1% exceeding 10 µg/dL. Assuming an absolute bioavailability of 50% (the NEPM default assumption) the IEUBK model predicts a geometric mean BLL of 2.4 ± 2.8 µg/dL with a range from 1.3 to 21.5 µg/dL (Table 3 and Fig. 4). Approximately 8.8% of the predicted BLLs exceed the NHMRC reference level of 5 µg/dL (NHMRC, 2015) and 2.3% exceed a BLL of 10 µg/dL, the former Australian guideline." Laidlaw et al. (2017) also stated that: "No difference in BLL was observed using measured Sydney median ANSTO air lead data from 2002 to 2006 and recently collected water lead in NSW (Harvey et al., 2016) compared with using default values from the NEPM (NEPM, 2013b)." Air Pb (and other metal) data for Sydney over the period 2002 to 2006 were described in Cohen et al. (2005).

3.1. Comparisons of dust loading and concentration

The outputs from these simulations are presented in Fig. 1. The differences between the observed PbB levels and predictions based on PDD concentration and with the "Succop" factor applied were significant at $p < 0.001$ (Wilcoxon signed-rank test for paired data). The difference between the observed values and those based on PDD loadings were significant at $p = 0.015$ for the aggregated observed + imputed data but were non-significant for the observed data ($p = 0.850$). The correlations between the observed and predicted values were approximately 0.40 in all four cases (Spearman rank-order correlation). The variability of the predictions for the observed + imputed data based on PDD loadings (inter-quartile range – IQR = 1.60) approximated that for the observed values (IQR = 1.30) while the variability of the other

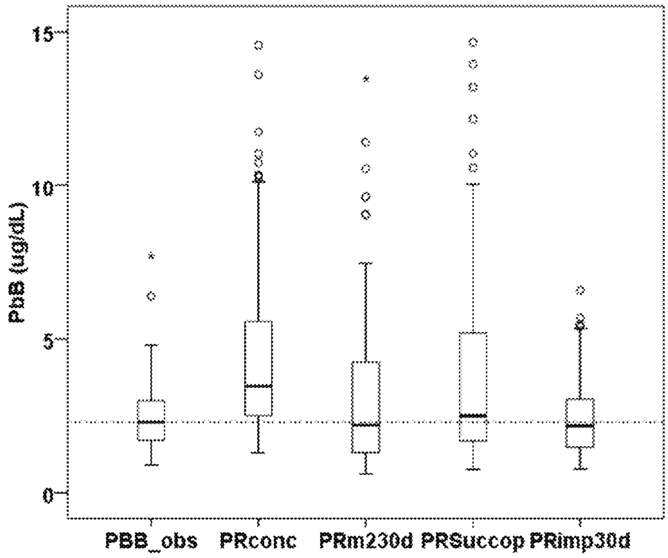

Fig. 1. Comparison of observed PbB (PBB_obs) with predicted (PR) PbBs using (i) PDD concentrations derived from the EPA conversion factor for loading and concentration (PRconc); (ii) PDD loading in µg/m^2/30days (PRm230d) using the aggregated data as in simulation 2, Table 1; (iii) PDD concentrations using the "Succop" factor (PRSuccop) from the aggregated data as in simulation 1, Table 1; and (iv) PDD loading from the aggregated observed + imputed data (PRimp30d) as in simulation 3 in Table 1. A reference line is drawn through the median value for the observed PbB data.

predictions were much larger (IQRs ranging from 3.25 to 3.72).

Based on these results we used predictions based on PDD loadings reported as µg/m^2/30 days for further individual and stratified age analyses and do not report predictions based on PDD concentration and with the "Succop" factor applied.

3.2. Predicted vs observed PbB values for aggregated data

To compare overall values of predicted PbB and observed PbB, the observed data for each child were aggregated over the 5-year interval of the study; site-specific data for an individual for only one time interval is the most common application of the IEUBK model. Observed and predicted PbB values for the aggregated data are illustrated in Fig. 2 for simulations of soil with PDD as loading (Soils + PDD in Fig. 2), sweepings with PDD as loading (Sweepings + PDD in Fig. 2) soil with (hand) wipes (Soil + Wipes in Fig. 2), and sweepings with (hand) wipes (Sweeps + Wipes in Fig. 2).

The similarity in outputs are consistent with those for the individual ages described in the following section. The geometric means are: 2.17 (± 1.24) µg/dL and median value of 2.21 µg/dL for soil with PDD; 1.95 (± 1.17) µg/dL and median value of 2.02 µg/dL for soil with handwipes; 2.36 (± 1.75) µg/dL and median of 2.25 µg/dL for sweepings with PDD, and 2.15 (± 1.69) µg/dL and median of 2.04 µg/dL for sweepings with handwipes. These results are in good agreement with the observed geometric mean PbB of 2.46 (± 0.99) µg/dL and median

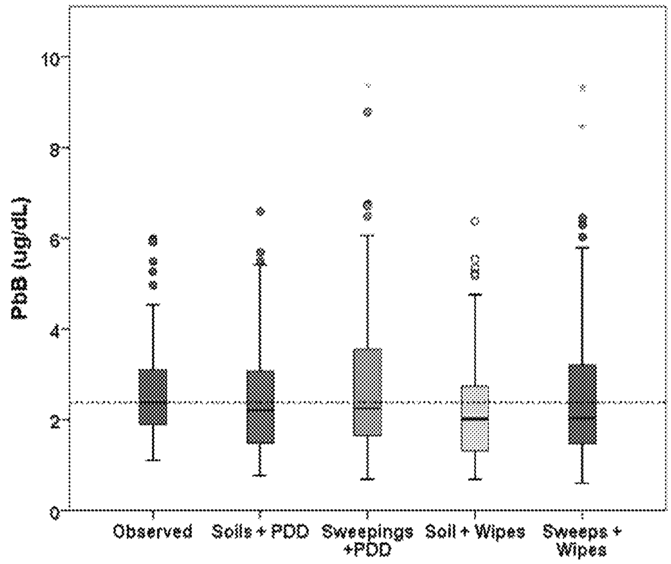

Fig. 2. Observed and predicted PbB values obtained with aggregated data for each child for soil with PDD as loading (Soils + PDD), sweepings with PDD as loading (Sweepings + PDD), soil with (hand) wipes (Soil + Wipes), and sweepings with (hand) wipes (Sweeps + Wipes). A reference line is drawn through the median value for the observed PbB data.

of 2.38 µg/dL although, as stated above, increasing the bioavailability to 50% gives small increases in geometric mean predicted PbB for soil with PDD of 2.3 µg/dL and 2.50 µg/dL for sweepings with PDD. The geometric means for soil with hand wipes remained unchanged.

The differences and the absolute differences between the observed PbB and predicted PbB are shown in Fig. 3. The differences were produced by subtracting the predicted from the observed values, as for residuals in regression analysis, but they are not referred to as residuals as their mean is not necessarily zero as it is in regression analyses. The average values of the absolute differences were compared using the Wilcoxon test. As can be seen, most of the differences were close to zero, with some exceptions. Wilcoxon tests showed that there was a significant difference between the observed values and the values predicted by the Model containing soil with hand wipes ($p < 0.001$), and soil and PDD ($p = 0.026$) but not those for the other two sets of predictors, based on sweepings and PDD or wipes. The absolute differences between observed and predicted values were significantly different for sweepings with wipes versus soil with PDD ($p = 0.020$), with those for the latter being smaller.

The correlations between the predicted and observed values were statistically significant for all the sets of predictors, but were not high, ranging from 0.371 (sweeps and wipes) to 0.401 (soil and PDD). The IQR for the observed values was 1.22, while the IQRs for the predicted values ranged from 1.46 to 1.93. The two greatest IQRs were for sweeps and wipes (1.93) and sweeps and PDD (1.77).

Overall, it would appear that simulations of the Model using alternative exposure measures of PDD and hand wipes instead of vacuum cleaner dust and dust sweepings instead of soil provide predicted PbBs whose median values are generally consistent with each other and those for observed values. The uniformly moderate correlations between the observed and predicted values show that there was less difference between the sets of predictors in terms of ordering individuals, and that the ordering did not closely match that of the observed values.

3.3. Observed and predicted PbB values for different age groups

In Fig. 4, the dark bars show the medians of the observed and predicted values of PbB, while the ends of the boxes show the 25th and 75th quartiles respectively. Plots for the individual age groups are illustrated in Supplementary Fig. S2a–f. The differences and absolute differences between the observed and predicted PbB values are shown in Figs. 5 and 6 respectively.

The median of the predicted PbB values was lower than that for the observed values for every combination of age and set of measures; in some cases, the difference was statistically significant. The differences were most likely to be significant for soil plus wipes ($p < 0.05$ for 4 to 5 year age groups) and least likely to be significant for sweeps plus PDD ($p < 0.05$ for 1 to 5 year age groups); two of the five differences were significant for the soil plus PDD and sweeps plus wipes. Comparing the significance of the differences between observed and predicted over age groups is harder to assess because of the different numbers in each group. However, while none of the four differences was significant in the under-1 group ($n = 32$), all were $p < 0.005$ in the 5 year-plus group

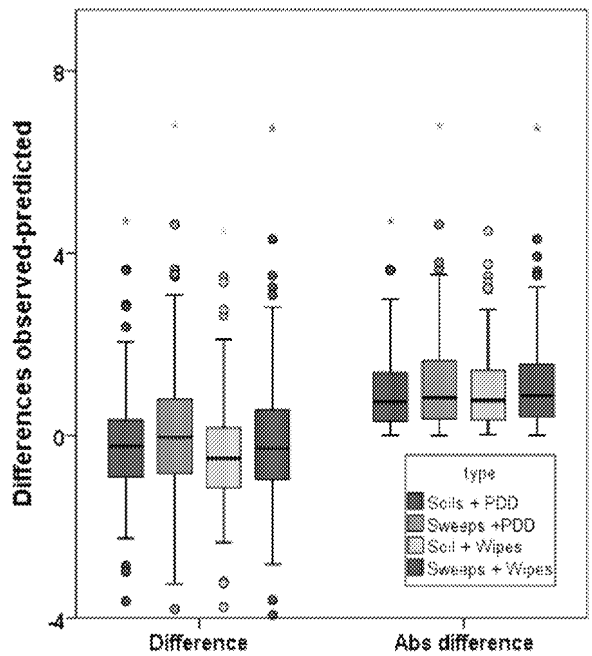

Fig. 3. Difference and absolute (Abs) difference between observed and predicted PbB values obtained with aggregated data for each child for Soil with PDD as loading (Soil + PDD), sweepings with PDD as loading (Sweeps + PDD), soil with (hand) wipes (Soil + Wipes), and sweepings with (hand) wipes (Sweeps + Wipes).

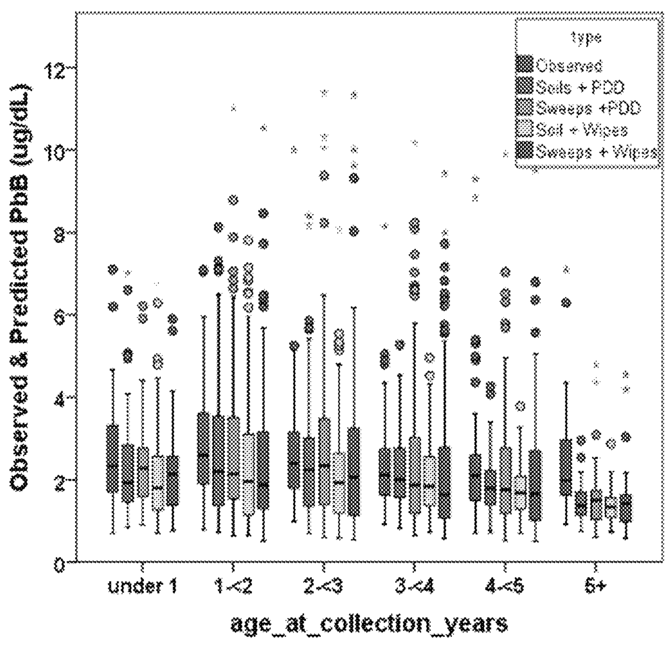

Fig. 4. Observed versus predicted PbB for soils with PDD (Soils + PDD), sweepings with PDD (Sweeps +PDD), soils with wipes (Soil + Wipes), and sweepings with wipes (Sweeps + Wipes) at the different ages of collection (years).

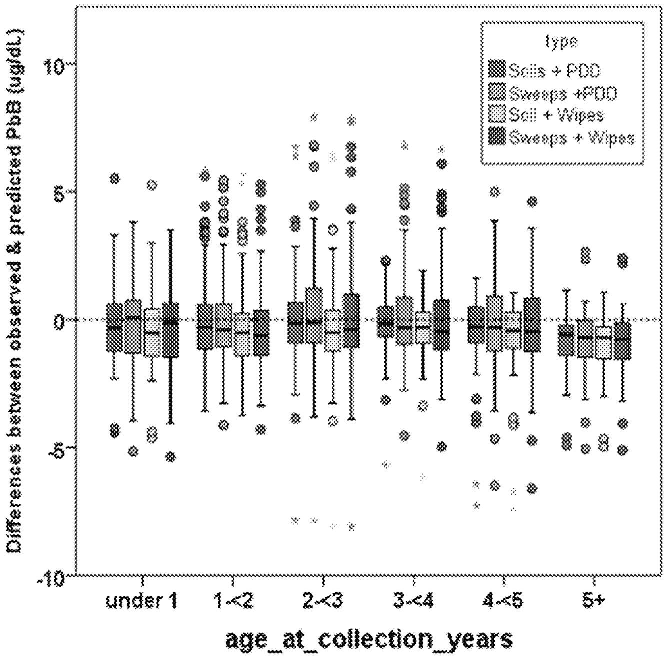

Fig. 5. Differences between observed and predicted values for Soils with PDD (Soils + PDD), Sweepings + PDD (Sweeps + PDD), Soils with handwipes (Soil + Wipes) and sweepings + handwipes (Sweeps + Wipes) at the different ages of collection (years). A reference line is drawn at zero difference.

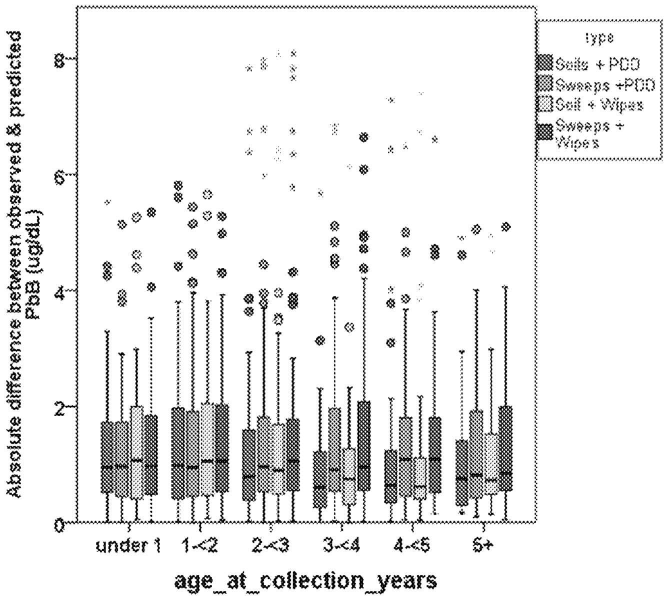

Fig. 6. Absolute differences between observed and predicted values for Soils with PDD (Soils + PDD), Sweepings + PDD (Sweeps + PDD), Soils with handwipes (Soil + Wipes) and sweepings + handwipes (Sweeps + Wipes) at the different ages of collection (years).

(n = 28). In the other age groups, one or two out of the four differences was significant.

To summarise, the differences between observed and predicted PbB tended to be greatest for the soil plus wipes measure and for the oldest age group.

The rank correlations between the observed and predicted PbB values ranged from 0.059 to 0.385. They were most consistently low to moderate for soil plus PDD (0.226–0.385) and soil plus wipes (0.135 to 0.366). They were more variable for sweeps plus PDD (0.059–0.385) and sweeps and wipes (0.065–0.359). The two lowest correlations occurred for the 4 - < 5 year old group, and the other correlations for this group were also low (0.226 and 0.135).

Generally, the variability of predicted values was greater than that of the corresponding observed values, although it was not very marked (the largest ratio of the IQR for predicted values to that for observed values was 1.7). In the under 1 year and 5 years or older groups, the IQRs for the predicted values were smaller than those for the observed values for all sets of predictors.

In general, the medians of the predicted values corresponded reasonably well to the medians of the observed values of PbB, but there was consistent underestimation. Significant differences between observed and predicted were least likely for predictions based on sweepings plus PDD. While the medians of predictions may be reasonable guides to the medians of observed values, it is evident that the ordering of individuals based on predictions may not may not correspond very well or at all with the ordering based on observed PbB values.

3.4. Modelling using default dust values in comparison with PDD and handwipe data

A situation often arises that specific site dust data are not available and in these cases a 'default' value for dust is calculated from the soil value in the IEUBK model (e.g. Biesiada and Hubichi, 1999; Laidlaw et al., 2017). The factor for the dust calculation is 0.7 of the soil Pb values. Using the observed aggregated data for each subject, we have modelled the predicted PbB using site-specific soil with their default dust values ('default dust') and compared these results with those obtained using soil with PDD and soil with handwipe data sets and the observed PbBs. The predicted PbB's for the 'default dust' modelling are overestimated compared with the observed PbB, and predicted values for soil with PDD and soil with handwipe (Fig. 7). For example, the average predicted PbB 'default dust' was 22% higher than that predicted by the soil with PDD data demonstrating the sensitivity of the soil inputs in predicting PbB using the Model. In using 'default dust' values with the IEUBK model, Biesieda and Hubichi (1999) obtained geometric mean predicted PbBs of 9.3 to 9.6 μg/dL in 4 Polish cities whereas the observed PbB geometric mean was 6.7 μg/dL.

3.5. Lead source allocations

Lead exposure can take place from ingestion, inhalation and dermal pathways although the latter is usually low (Stauber et al., 1994) and is not taken into account in our study. Exposure for inhalation is measured by air and ingestion measured by diet, water and soil/dust. The

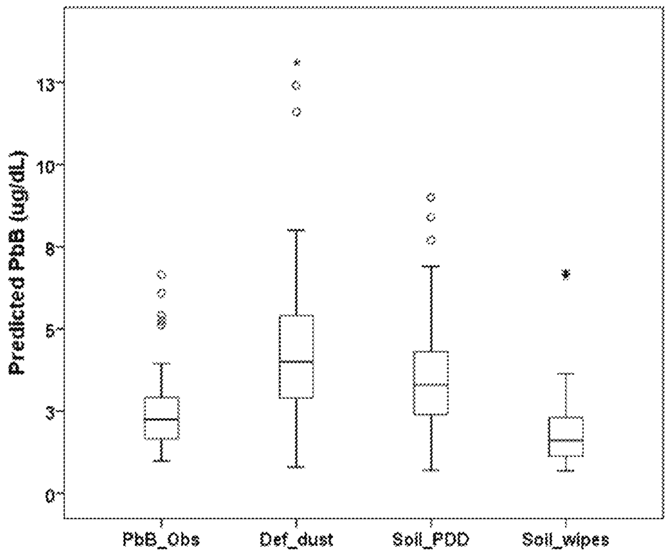

Fig. 7. Predicted PbBs using 'default dust' (Def_dust) data calculated from the soil values compared with the observed PbB (PbB_Obs) and predicted PbBs from soil with PDD (Soil_PDD) and soil with hand wipes (Soil_wipes) simulations for subjects 4001 to 4060 at an age from 2–3 years. Using soil only data significantly overestimates PbBs.

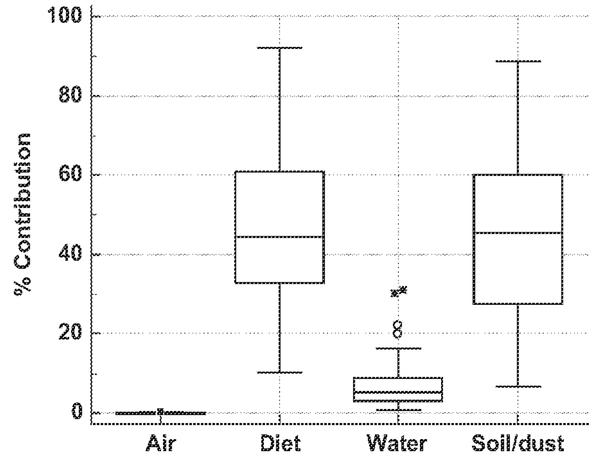

Fig. 8. Lead source allocations of IEUBK Pb prediction for environmental exposures for a child 1–2 years of age.

relative contributions to predicted PbB levels in the Sydney children at ages 1–2 years from different exposures as inputs to the IEUBK model are shown in Fig. 8 using the aggregated data for each subject. The results show that compared with total Pb intake, dietary and soil/dust contribute equally to PbB levels with geometric means of 42% and ranges of 10–92% for diet and 7–89% for soil/dust (Fig. 8). The contributions from air and water are low at 0.09% and 5.3% respectively. The mean values are quite different from those reported for Chinese cities by Li et al. (2016) of 83% (57–94%) for diet and 15% (3–42%) for soil/dust and Zhong et al. (2017) of 73 ± 12% for diet and 25 ± 11% for soil/dust but all three studies demonstrate the importance of diet to total Pb intake using IEUBK modelling.

4. Discussion

4.1. IEUBK results

In the IEUBK modelling, no adjustment is made for other variables such as risk and gender although in the mixed model analyses described in Section 4.3 traffic proximity (risk) is rarely significant.

Hence if PbB is predicted using soil values and default values for the other variables including calculating dust from the soil values, this is equivalent to the unadjusted analyses for soil only and over-estimates the significance of soil versus PbB. The approximately equal contributions of diet and soil/dust Pb intake compared with total intake were rather unexpected given the abundance of papers promulgating the importance of soil/dust to PbB levels in children. In contrast to the results for soil/dust from the modelling the mixed model analyses (Section 4.3) showed that the variance without dust sweepings and soil was 1.6% (compared with 4.6% when included in the model), indicating their lower contribution to the overall variance. This contrasts with higher variance soil contributions up to 75% in studies using very large data bases such as that of Zahran et al. (2013b) with 55,551 children in New Orleans, but these statistical analyses did not adjust for dust, diet, etc.

4.2. Comparison with other studies

The IEUBK model has been widely used in risk assessment especially in the US for remediation of mining and smelting in the US (e.g., von Lindern et al., 2003a, 2003b, 2016; Brattin and Griffin, 2011; Griffin et al., 1999; Goodrum et al., 1996; Hogan et al., 1998; Tsuji and Serl, 1996; Lee et al., 1995). The best-known site is the Bunker Hill Superfund site in Idaho and has been the subject of long-standing investigations and many papers by the TerraGraphics group (e.g., von Lindern et al., 2003a, 2003b, 2016). Soil and dust ingestion rates and bioavailability are sensitive parameters in the IEUBK model and in their latest paper, von Lindern et al. (2016) re-evaluated these variables for Bunker Hill as von Lindern et al. (2003a) suggested that IEUBK default soil/dust ingestion rates overestimate the mean PbB, primarily in the upper age ranges.

Outside the USA, the IEUBK model has been used in mining/smelting/urban sites, for example, in China. A comprehensive investigation around a battery factory and Pb-zinc mine in Central China by Li et al. (2016) of 760 children aged 61–84 months used measurements of PbB (venepuncture) and environmental samples including air, drinking water, soil, dust and diet (estimated from the Chinese National Nutrition and Health Survey of Year 2002) along with site-specific time-activity patterns. The authors used exposure parameters of indoor and outdoor activity time, ventilation rate and water consumption that were different to the default values of the IEUBK model. They found no statistical difference using Student's *t*-test between the predicted and observed BLLs ($t = 1.488$, p 0.152) and a Pearson correlation of r 0.91, $p < 0.001$. The average predicted to observed PbB ratio was 1.00 with a range of 0.78–1.26. Soil/dust Pb contributed approximately 15% (3–42%) to total Pb intake and diet was the dominant contributor at 83% (57–94%).

In a similar study of 14 cities in China, Zhong et al. (2017) used a Monte Carlo module with the IEUBK model to predict PbB. Only studies published between January 2005 and January 2016 and with a sample size larger than 500 were selected. The exposure data were obtained from the China National Knowledge Infrastructure and Web of Science so were not necessarily subject/site-specific. Blood Pb data were combined to one value by taking sample-size weighted geometric mean and geometric standard deviation as representative of PbB levels for each city or region. The average predicted to observed PbB ratio was 0.93 with a range from 0.86 to 1.03 and on a linear plot the R^2 was 0.94. As with the above study, diet was the dominant contributor to total Pb uptake with values of 73 ± 12% (range 32–90%)and soil/dust was 25 ± 11% (range 9–63%). The authors suggested that the Pb contribution from diet may be overestimated because of limited Pb uptake from dietary consumption (Li et al., 2016). Lead uptake from diet, assuming 50% bioavailability as the default value in the Model, ranged from 10.3 to 13.6 µg/day which is roughly twice that observed in our Sydney study (geometric mean 5.9 µg/day; n 832).

In contrast to the high correlations in the Chinese studies, Bowers and Mattuck (2001) modelled data from three US smelter communities and the urban center of Cincinnati. The IEUBK-predicted geometric mean PbB was greater than the observed geometric mean for the smelter sites but not for Cincinnati (their Table 2, page 1703). Plots of the observed to predicted PbB showed considerable scatter especially as the plots were log scale (their Fig. 1).

The Model has been less well applied in other urban environments and commonly only limited site-specific exposure data have been incorporated into the modelling (e.g. Stewart et al., 2014; Hu et al., 2013; Wang et al., 2011; Laidlaw et al., 2017). Wang et al. (1997) used the Model for 70 complete data sets of environmental Pb and PbB in 2-year-old children measured in 1984/1985 in Birmingham, UK and found the predicted Pb of 11.5 µg/dL for 1984/1985 closely matched the observed value of 11.6 µg/dL for 2-year-old children. Deshommes et al. (2013) used the Model in a study focussed on Pb service water lines (LSL) to residences in Montreal Canada. They found a GM PbB of 1.2 µg/dL was measured for children living in homes without an LSL, while a GM PbB of 1.5 µg/dL was measured for children living in homes with an LSL, with all ages combined. Their IEUBK PbB predictions for homes without an LSL (0.77–1.8 µg/dL) fell within the 1.2 µg/dL GM measured in Montreal children. Conversely, the PbB levels modelled for single homes with an LSL in winter (1.5–2.5 µg/dL) exceeded the observed PbB levels. The authors thought the observed difference may be explained by the input parameters to the Model, particularly the relatively high daily water intake (742–1000 mL/d). Site-specific observed PbB data have not been available in several of the studies (e.g. Stewart et al., 2014; Laidlaw et al., 2017).

Even though widely used and said to be validated by several groups, there remains controversy over the validity of the Model. For example, Bowers and Mattuck (2001) suggested that PbB levels for two smelting sites of Midvale (Utah) and Sandy (Utah) and the urban site of Cincinnati Ohio are 'not well represented by the Model's predictions'. They further state that "This reduces the value of the Model for use in communities where PbB measurements have not been made, and suggests that caution should be exercised when using the Model to set soil cleanup levels or to predict the result of remediation". In one of the few urban studies, Goodrum et al. (1996) used Monte Carlo modelling (ISE/IEUBK) with the IEUBK model for children from Syracruse New York and found that both models tend to under-predict the observed geometric mean PbB. In contrast, in 4 cities in Poland, Biesiada and Hubicki (1999) found a predicted geometric mean PbB of 9.3 µg/dL whereas epidemiological data had a geometric mean of 6.6 µg/dL. Brattin and Griffin (2011) concluded that the average mass fraction of soil in dust (of 0.7) may not be constant and there is "value in collecting paired measurements of lead in soil and dust (at Superfund sites) in order to improve the accuracy of human health risk assessment for lead."

4.3. Mixed model analyses for blood and environmental samples (from Gulson et al., 2014)

In an analysis with PbB as the dependent variable and with the adjusted predictors, none was individually statistically significant (Supplementary Fig. S3) which was as expected, given the strong correlations among the predictors. There was a marginally significant association of PbB and interior house dust and soil. Moreover, individually (unadjusted) the predictors showed some significant associations with PbB (Supplementary Fig. S4).

An evaluation of the impact of the predictor variables on the blood results showed that the percentage of the variance explained by the predictors (calculated using the method described by Snijders and Bosker, 2012) was low at 9% for Pb. Compared with the full model, the variance explained without diet, interior hand wipes and exterior dust sweepings is 4.6%, indicating a substantial contribution of the variance arising from these variables. Compared with the full model, the variance without dust sweepings and soil was 1.6%, indicating their lower contribution to the overall variance. This is at variance with the IEUBK modelling which indicates that the soil and dust geometric mean contribution to total intake was about 42% (see Section 3.5 above) and a similar value was observed for diet. The latter contrasts with mixed model analyses that showed diet was not a significant contributor to PbB in these children with an estimate of 0.016 and p of 0.2 (Supplementary Fig. S3).

In the analysis of a possible association of interior hand wipes with interior house dust accumulation/ soil/ dust sweepings, interior dust Pb and soil Pb predicted the Pb in interior hand wipes (Supplementary Fig. S3). Unadjusted interior house dust, dust sweepings and soils predicted the Pb in hand wipes (Supplementary Fig. S4) but all three measures were highly correlated. As with interior hand wipes, there were significant associations for exterior hand wipes, after playing outside, with Pb in interior house dust and marginally with soil but unexpectedly not with exterior dust sweepings. There were no significant relationships between Pb and traffic proximity.

There was a significant association between the interior house dust and dust sweepings. There was a significant association of the sweepings and soil and there was a significant association for Pb and traffic proximity. There were no seasonal effects for Pb. An evaluation of the impact of the predictor variables on the dust sweeping results shows the percentage of the variance explained by the predictors was 26% for Pb.

4.4. Using the predicted values for decision-making

In a practical setting, the PbB levels obtained from models such as those considered here could be used to decide whether a child and its environment should be monitored if their PbB are above current guidelines although in practice, this would be misuse of the IEUBK model as it was developed to predict population PbB distributions and not PbB levels of individuals. However, even experts commonly use the phrase such as in the IEUBK model "..seeks to predict the probability **a child** would have an elevated BLL" (Peer Reviewers Question EPA Drinking Water Lead Modelling Approaches, INSIDEEPA.com, 2017, page 2). The EPA Directive states: "…generally, OSWER will attempt to limit exposure to soil lead levels such that a typical (or hypothetical) child or group of similarly exposed children would have an estimated risk of no more than 5% of exceeding a 10 µg/dl blood lead level." (https://www.epa.gov/sites/production/files/documents/pbpolicy.pdf)

One way of evaluating the individual predictions based on the Model is use them with a cut-off which might be applied to decide whether the level of PbB is high enough to require action such as remediation or ongoing monitoring. If we use one of the prediction combinations which produced estimates closest to the observed values, sweeps plus wipes, and adopt a cutoff of 5 µg/dL, the current reference level, we find that 11, or 10.2%, of people would require follow-up. The number of people whose observed PbB levels would require action with a criterion of 5 is 4, or 3.7%. We can examine the relationship between the decisions based on the two measures in terms of "hits", the percentage of those at or above the criterion in terms of the observed measure who meet the same criterion on the predicted measure, which is 2, or 50%. The other relevant index is the percentage of "false alarms", and that is 8.7% (the percentage who did not meet the criterion on the observed measure but who did so on the predicted measure), nine people. The numbers of cases are too small for this result to be reliable, but the analysis suggests a way that the results could be evaluated in practical terms.

4.5. Limitations

Instead of house dust from vacuum cleaning, we have used dust fall accumulation with petri dishes which provide information about exposure over time but which have dust loading units of µg/m^2/30 days. Likewise, we have explored hand wipe data for the children instead of house dust in the modelling. Nevertheless, predicted PbB values from the Model simulations using these exposures give reasonable agreement with observed PbB values. On the other hand, the simulations using loading give better agreement with observed PbB than when the loadings are converted to concentration. In both cases, the particle size of the PDD and hand wipe materials is < 150 µm and are a 'worst case' scenario as far as children's exposure is concerned. With respect to hand wipe data, these were taken when the other sampling was done and recorded in µg Pb per hand wipe. Hence these measurements have to be the most unreliable with respect to daily intake; for example, they would be minimal values if the hands were washed just prior to the other sampling.

Our study used soils which were sieved to < 2 mm whereas the new guidelines for particle size for soils recommend a size of < 150 µm (US EPA, 2016). This is because it has been recognised for several decades that finer particle sizes have higher metal concentrations than coarser particles and finer material adheres more tightly to hands and so is more readily available for hand-to-mouth activity in children. Hence our use of the < 2 mm size soil fraction with lower Pb contents would result in lower predicted PbBs than for a finer soil particle size and may be part of the explanation for the slightly lower predicted PbBs in the Model simulations compared with observed PbBs.

5. Conclusions

Simulations with the IEUBK model using alternative environmental measures for dust exposure of dust fall accumulation with petri dishes or hand wipes and exterior sweepings instead of soil produce predicted PbBs which agree encouragingly well with each other and with the observed PbB. Likewise, the first trials, to our knowledge, with site-specific exposure measures stratified for 6 different age ranges indicate that differences between observed and predicted PbB tended to be greatest for the soil plus wipes measure and for the oldest age group.

Simulations for each subject using data aggregated over the 5-year interval of the study gave better agreement in predicted PbB for each sampling group than for the stratified data. There were no significant differences among the absolute differences between the predictions and the observed PbB levels. Simulations involving a single site-specific set of measurements for each individual have been the usual approach in using the IEUBK model.

In simulations, analogous to situations where site-specific dust values are not available and default dust values are estimated from the soil concentrations, the predicted/observed values are overestimated by 22% in comparison with soil with PDD results and about 50% by comparison with soil with hand wipes results. These overestimations are similar to outcomes found by other researchers and conclusions derived from such modelling.

Finally, we think the conclusions about dust lead and children's PbB of Emond et al. (1997) are relevant to our study: "Variation in lead deposition within small areas and variations in collection inherent to the devices are the major contributors to measurement error. Measurement error causes dramatic underestimation of correlation between lead-contaminated house dust and children's blood lead."

It would be interesting to see results from other IEUBK modelling studies where different site-specific data for dust are available such as surface wipes.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2017.10.040.

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